(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
23 October 2003 (23.10.2003)

PCT

(10) International Publication Number
WO 03/087081 A1

(51) International Patent Classification[7]: C07D 307/87, C07C 69/63, 33/46, 69/16

(21) International Application Number: PCT/CA03/00522

(22) International Filing Date: 8 April 2003 (08.04.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
2,381,341 9 April 2002 (09.04.2002) CA

(71) Applicant *(for all designated States except US)*: **TORCAN CHEMICAL LTD.** [CA/CA]; 110 Industrial Parkway North, P.O. Box 308, Aurora, Ontario L4G 3H4 (CA).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: **TSE, Hoi, Lun, Allan** [CA/CA]; Unit 1, Crockhamhill Drive, Scarborough, Ontario M1S 3H1 (CA).

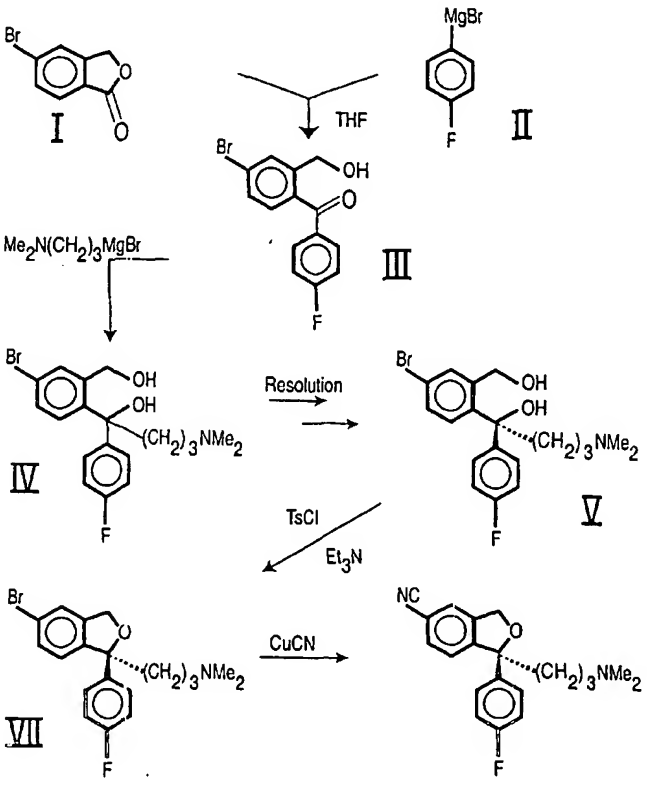
(74) Agents: **JOACHIM, Roland, H.** et al.; Ridout & Maybee LLP, One Queen Street East, Suite 2400, Toronto, Ontario M5C 3B1 (CA).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: PROCESS AND INTERMEDIATES FOR PREPARING ESCITALOPRAM



(Escitalopram)

(57) Abstract: The antidepressant drug Escitalopram is prepared from 5-bromophthalide via the diol intermediate (4-bromo-2-(hydroxymethyl)phenyl)-(4-fluorophenyl)methanol.
The racemic diol intermediate is converted to an enantiomerically enriched form by first converting the diol to a monoester intermediate and then reacting the monoester intermediate with an optically active acid, most preferably (+)-di-p-toluoyl tartaric acid, to form a salt. The salt is then crystallized to recover an enantiomerically enriched, crystalline form thereof. The monoester intermediate is preferably formed by reacting the racemic diol intermediate with an acid or a reactive acid derivative which, in a particularly preferred embodiment, is acetic anhydride.

WO 03/087081 A1